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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/591,990

10/20/2006

Yoshio Umezawa

2006_1514A

3080

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7590

09/16/2009

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EXAMINER

PROUTY, REBECCA E

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

09/16/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/591,990	Applicant(s) UMEZAWA ET AL.	
	Examiner Rebecca E. Prouty	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 5-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 9/7/06 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/06</u> | 6) <input type="checkbox"/> Other: _____ |

Applicant's election without traverse of Group I, claims 1-4 in the reply filed on 7/24/09 is acknowledged.

Claims 5-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/24/09.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 are confusing in the recitation of "pair of probes" as it is unclear how one determines when two independent things comprise a "pair". The term "pair" implies intended use together. However, the intended use of a product is not a limitation on the product itself and thus there is no way to define when two things constitute a pair. If applicants intend to recite a "kit", i.e., two products which are packaged together then they are suggested to amend the claims accordingly.

Claims 1 and 2 (from which claims 3 and 4 depend) are indefinite in the recitation of "C-terminal side polypeptide of an intein", "C-terminal side polypeptide of a reporter protein",

"remaining N-terminal side polypeptide of the intein", and "remaining N-terminal side polypeptide of the reporter protein" as inteins and reporter proteins are not comprised of polypeptides. It appears that applicants intended meaning is in fact "C-terminal fragment of an intein", "C-terminal fragment of a reporter protein", "remaining N-terminal fragment of the intein", and "remaining N-terminal fragment of the reporter protein". Amendment as such is suggested.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 4 are rejected under 35 U.S.C. 102(a) as being anticipated by Kim et al. (Reference AO of applicants IDS)

Kim et al. teach a pair of probes for detecting protein ligand induced nuclear transport of the androgen receptor wherein the first probe comprises a fusion protein comprising in N-terminal to C-terminal order a C-terminal fragment of a DnaE intein, a C-terminal fragment of *Renilla* luciferase and the androgen receptor and the second probe comprises in N-terminal to C-terminal order the remaining N-terminal fragment of the

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DnaE intein, the remaining N-terminal fragment of the *Renilla* luciferase and a nuclear localization signal. (See Figure 1).

Claims 2 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Ozawa et al.

Ozawa et al. teach a pair of probes for detecting mitochondrial transport of a protein of interest wherein the first probe comprises a fusion protein comprising in N-terminal to C-terminal order a protein of interest, an N-terminal fragment of a DnaE intein, and an N-terminal fragment of enhanced GFP (EGFP) and the second probe comprises in N-terminal to C-terminal order a mitochondrial targeting sequence (MTS), the remaining C-terminal fragment of the DnaE intein, and the remaining C-terminal fragment of the EGFP. (See Figure 1). The probes of Figure 1 of Ozawa et al. differ from those of claim 2 and 3 only in the replacement of the mitochondrial targeting sequence with a nuclear targeting sequence. However, Ozawa et al teach that the probes disclosed would allow for identification not only of proteins localized to mitochondria but also in the nucleus, ER , Golgi or peroxisome by replacing the MTS attached to the remaining C-terminal fragment of the DnaE intein, and the remaining C-terminal fragment of the EGFP with the targeting signals for the desired organelle (see page 292). Thus Ozawa et al. teach probes in which the MTS is of the

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second probe is replaced with a nuclear targeting signal. This disclosure anticipates the instant probes.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 2 rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (Reference AO of applicants IDS).

Kim et al. is described above. The only difference between the disclosure of Kim et al. and claim 2 is that in Kim et al. the nuclear localization signal is attached to the N-terminal fragments of the intein and reporter protein and the androgen receptor to the C-terminal fragments of these proteins while in claim 2 they are reversed (i.e., the nuclear localization signal is attached to the C-terminal fragments and the androgen receptor to the N-terminal fragments). However, one of ordinary

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skill in the art would readily understand that in the disclosed system of Kim et al. what is important is that the nuclear localization signal and androgen receptor be attached to separate probes such that the probes be initially directed to separate cellular compartments but that either portion of the split intein and split reporter protein could be located in either intracellular compartment as they will only reconstitute a full intein/reporter protein when brought into close proximity regardless of where each portion is initially located.

Therefore it would have been obvious to one of ordinary skill in the art to modify the probes of Kim et al. to attach the nuclear localization signal to the C-terminal fragments of the intein and reporter protein and the androgen receptor to the N-terminal fragments thereof as a skilled artisan would have recognized that which portion of the split intein/reporter protein these elements are attached to is a mere matter of design choice among functionally equivalent options as long as each of them is attached to different portions of the split enzyme/reporter protein.

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ozawa et al. in view of Paulmurugan et al.

Ozawa et al. is described above. The only difference between the disclosure of Ozawa et al. and claim 1 is that in

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Ozawa et al. the nuclear localization signal is attached to the C-terminal fragments of the intein and reporter protein and the protein of interest to the N-terminal fragments of these proteins while in claim 1 they are reversed (i.e., the nuclear localization signal is attached to the N-terminal fragments and the protein of interest to the C-terminal fragments). Ozawa et al. differs from claim 4 only in that the split reporter protein used by Ozawa et al. split EGFP while claim 4 recites that the reporter enzyme is a luciferase.

Paulmurugan et al. teach a split *Renilla* luciferase protein complementation system for detecting protein-protein interactions and that *Renilla* luciferase is a highly suitable reporter protein for split enzyme systems as it is a monomeric protein of small size (36KD) and does not require ATP or post translational modification for activity.

Therefore, it would have been obvious to one of ordinary skill in the art to modify the probes of Ozawa et al. to replace the split EGFP reporter protein with the split *Renilla* luciferase protein fragments taught by Paulmurugan et al. as Paulmurugan teach the advantages of using *Renilla* luciferase in split enzyme systems.

Furthermore, one of ordinary skill in the art would readily understand that in the disclosed system of Ozawa et al. what is

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important is that the localization signal for targeting to the desire organelle (i.e., MTS, nuclear localization signal or targeting signal for other organelles) and the protein of interest be attached to separate probes such that the probes be initially directed to separate cellular compartments but that either portion of the split intein and split reporter protein could be located in either intracellular compartment as they will only reconstitute a full intein/reporter protein when brought into close proximity regardless of where each portion is initially located. Therefore it would have been obvious to one of ordinary skill in the art to modify the probes of Ozawa et al. to attach the nuclear localization signal to the N-terminal fragments of the intein and reporter protein and the protein of interest to the C-terminal fragments thereof as a skilled artisan would have recognized that which portion of the split intein/reporter protein these elements are attached to is a mere matter of design choice among functionally equivalent options as long as each of them is attached to different portions of the split enzyme/reporter protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
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